RVD2008-05

Re-evaluation Decision

Oxamyl

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Re-evaluation Decision

After a re-evaluation of the insecticide oxamyl, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting continued registration of oxamyl products for sale and use in Canada.

An evaluation of available scientific information found that, under the proposed conditions of use, products containing oxamyl do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of oxamyl uses, new risk-reduction measures must be included on the label of products containing oxamyl.

- Personal protective equipment (PPE) is required when handling products containing oxamyl. Custom application to potatoes requires additional mitigation when handling more than 110 kg a.i./day using closed mix/load equipment (with coveralls and gloves) and closed cab ground application equipment.

- Restricted-entry intervals (REIs) of one day for non-bearing apple trees and three days for raspberries and potatoes are required.

- The maximum application rate for foliar application to non-bearing apple trees must be reduced from 2.244 kg a.i./ha to 1.68 kg a.i./ha.

- The number of applications must be restricted to two per season for potatoes and three per year for non-bearing apple trees with a minimum interval of 14 days between applications.

- Observance of buffer zones is required to protect non-target aquatic habitats from spray drift.

- Advisory statements as precautionary measures are required on product labels to minimize the risk of aquatic contamination from surface runoff.

The regulatory approach for oxamyl was first proposed in the consultation document[1] *Proposed Re-evaluation Decision—Re-evaluation of Oxamyl* (PRVD2007-02). This Re-evaluation Decision document[2] summarizes the Agency's decision and the reasons for it. Appendix I summarizes the comments received during the consultation process and the PMRA's response to these comments. The information did not result in substantive changes to the assessment in PRVD2007-02. Therefore, this decision is consistent with the proposed re-evaluation decision stated in PRVD2007-02. To comply with this decision, registrants of oxamyl products will be informed of the specific requirements affecting their product registration(s) and of regulatory options available to them.

For more details on the information presented in this Re-evaluation Decision, please refer to the related PRVD2007-02 (www.pmra-arla.gc.ca/english/pdf/prvd/prvd2007-02-e.pdf).

Other Information

For oxamyl, comments on PRVD2007-02 did not result in significant changes to the science assessments. Therefore, the summary of assessments found in PRVD2007-02 serves as an evaluation report. A list of references considered by the Agency in support of the registration decision are found in Appendix II. The relevant test data on which the decision is based are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[3] regarding this decision on oxamyl within 60 days from the date of publication of this Re-evaluation Decision document. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Request a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html), or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

1.0 Comments on Toxicology Assessment—Oncogenicity study

A registrant challenged the assessment of the acceptability of the mouse carcinogenicity study and the subsequent application of an additional uncertainty factor for the dermal and inhalation endpoints used in the intermediate-term occupational risk assessments. The registrant has submitted an in vivo Mouse Bone Marrow Micronucleus Assay as further evidence to support the lack of genotoxicity in the database.

PMRA Response

The PMRA agrees that there is no evidence of carcinogenicity observed in this mouse study. This is supported by the negative chronic/carcinogenicity study in the rat as well as the negative genotoxicity database. However, the carcinogenicity study in the mouse is considered supplemental due to study deviations.

According to the Organisation for Economic Co-operation and Development's guideline 451 for carcinogenicity studies, "... in order for a negative test to be acceptable, it should meet the following criteria: (1) No more than 10 percent of any group is lost due to autolysis, cannibalism or management problems; (2) Survival of all groups is no less than 50 percent at 18 months for mice." The PMRA concurs with the registrant that there is an adequate number of surviving mice in each group at 18 or 24 months (greater than 56% or 35%, respectively) and that the study was carried out longer than required. However, while the PMRA agrees that many animals were unaffected by autolytic changes, the number of animals with whole body autolysis (greater than 18% in all treatment groups) is unacceptable for a negative test. Whole body autolysis occurred primarily in animals found dead, which represented the most sensitive members of the population. Exclusion of the full histopathology of these animals leaves residual uncertainty about the carcinogenic potential of oxamyl. The high percentage of mice with whole body autolysis prevented an adequate number of animals from being examined histologically in some organs. This study remains unacceptable to satisfy the requirement of a rodent carcinogenicity study. In addition, there is no subchronic study in the mouse to verify that the target organs were adequately examined in the carcinogenicity study. The PMRA considers that there remains uncertainty about the carcinogenic potential of oxamyl, since there is neither an acceptable subchronic nor carcinogenicity study in the mouse.

An in vivo Mouse Bone Marrow Micronucleus Assay was submitted as further evidence to support the lack of genotoxicity in the database. This study will be evaluated to determine acceptability when there is a request for expanded use of oxamyl.

1.1 Comments on Toxicology Assessment—Toxicology Endpoint Selection for Occupational and Residential Risk Assessment

A registrant considered that the 3-fold extra uncertainty factor added to the margin of exposure (MOE) for the intermediate-term dermal and inhalation risk assessments should be removed if the mouse carcinogenicity study is considered acceptable.

PMRA Response

The mouse carcinogenicity study remains unacceptable so the 3-fold extra uncertainty factor for intermediate-term dermal and inhalation risk assessments is still required.

2.0 Comments on Postapplication Exposure and Risk Assessment—Proposals Pertaining to Occupational/Residential Exposure

A registrant proposes that the 3-fold extra uncertainty factor is not necessary for intermediate-term exposures based on the acceptability of the mouse carcinogenicity study. If the additional 3-fold factor is removed, the intermediate-term risk assessment for the application of oxamyl to potatoes would be acceptable when assessed with coveralls over a single layer of clothing, chemical-resistant gloves and a respirator (open mixing/loading, open cab application) and a treated area of 300 ha/day. The estimated aggregate risk index (ARI) for the combination of dermal and inhalation MOEs under these conditions is approximately 1.7. It is also proposed that the determination of REIs be reassessed for intermediate-term exposures using a target MOE of 100.

PMRA Response

The acceptability of the mouse carcinogenicity study has been discussed and it was concluded that the extra 3-fold uncertainty safety factor is required. As such, the occupational and postapplication exposure risk assessment remains unchanged at this time, and all proposed risk mitigation measures outlined in the Proposed Acceptability for Continuing Registration document are required.

3.0 Comments on Environmental Risk Assessment—Statement Pertaining to Foraging Bees

Section 4.7 of the PRVD is not clear regarding application of oxamyl while bees are foraging.

PMRA Response

The current registered label includes a statement regarding reducing hazard to bees. This is sufficient to address the mitigation described, and therefore additional label statements do not appear in Appendix VI, Label Amendments for Commercial Class Products Containing Oxamyl, of the PRVD.

Appendix II List of References

Studies/Information Provided by Applicant/Registrant

PMRA Number	Reference
1449524	2002, Oxamyl (DPX-D1410) Technical (98% w/w): Mouse Bone Marrow Micronucleus Assay, DuPont-10618, MRID: NA, DACO: 4.5.7
1437182	Response to Review by Lab Services, Agriculture Canada- March 6, 1989., DACO: 0.8,2.13.3
1437191	1988, Response to Review by Lab Services, Agriculture Canada- March 6, 1989. CONFIDENTIAL ATTACHMENT: Oxamyl: Vydate L and Oxamyl Technical 42. Analysis and Certification of Product Ingredients., D1410.F, DACO: 2.13.3 Occupational
1053109	U.S. EPA, 1999a. Memo: R. Sandvig to C. White and D. Locke. Review of *"Dissipation of Dislodgeable Foliar Residues of Oxamyl from Citrus Following Application of Vidate L Insecticide in the USA - Season 1997"*.PC Code 103801. MRID 446869-01. Office of Prevention, Pesticides and Toxic Substances. Washington, DC. pp. 14. October 29, 1999.
1053120	U.S. EPA, 1999b. Memo: R. Sandvig to C. White. Secondary Review of *"Dissipation of Dislodgeable Foliar and Soil Residues of Oxamyl Following Application of Vidate L Insecticide to Tomatoes in the USA - Season 1997 and 1998"*.PC Code 103801. MRID 447048-01. Office of Prevention, Pesticides and Toxic Substances. Washington, DC. pp. 15. October 29, 1999.
1053115	U.S. EPA, 1999c. Memo: R. Sandvig to C. White and D. Locke. Review of *"Dissipation of Dislodgeable Foliar Residues of Oxamyl from Cucumbers Following Application of Vidate L Insecticide in the USA - Season 1997"*. PC Code 103801. MRID 446869-02. Office of Prevention, Pesticides and Toxic Substances. Washington, DC. pp. 17. October 29, 1999.
271256	U.S. EPA, 2000. Data Evaluation Record for Oxamyl. Acute Oral Neurotoxicity - Rat. PC Code 103801. MRID Numbers 44254401, 44420301, 44740701, 44628701 - 446287030, 44660601. Oak Ridge National Laboratory, Oak Ridge, TN. pp. 18. February 3, 2000.

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1341388 Long Term Feeding Study in Mice with Oxamyl. Summary and Appendices A,D,G,I,J,K,N. Haskell Laboratory Report No. 25281. WIL Research Laboratories, Inc. WIL 77033/HLO-252-8l/MR-2799-001. pp. 266. June 22, 1981.

1341389 Long Term Feeding Study in Mice with Oxamyl. Appendix B. Haskell Laboratory Report No. 25281. WIL Research Laboratories, Inc. WIL 77033/HLO-252-8l/MR-2799-001. pp. 255. June 22, 1981.

1341390 Long Term Feeding Study in Mice with Oxamyl. Appendix H. Haskell Laboratory Report No. 25281. WIL Research Laboratories, Inc. WIL 77033/HLO-252-8l/MR-2799-001. pp 98. June 22, 1981.

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1343849 Oral LD50 Test. Haskell Laboratory Report No. 214-69. pp 2. July 31, 1969.

1343850 Ten-Dose Subacute Oral Test. Haskell Laboratory Report No. 220-67. pp 2. June 25, 1968.

1343852 Eye Irritation Test on Rabbits. Haskell Laboratory Report No. 263-68. pp 2. November 18, 1968.

1343854 Acute Skin Absorption Toxicity Tests on Rabbits. Haskell Laboratory Report No. 282-70. pp 4. December 30, 1970.

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1343860 Acute Dust Inhalation Toxicity. Hazleton Laboratory Report No. 280-69. pp. 3. December 18, 1972.

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Additional Information

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